REMARKS

Claims 1 and 4 are amended to be consistent with claims 2 and 3, formally reciting the antecedent "test MIF concentration". It is inherent that the second "assessment making" step is made in accordance with the first step, which determines the MIF concentration. This amendment does not change the scope or subject matter of the claims, and introduces no new matter.

Finality

We request withdrawal of the finality of the Action dated 7/14/06 because our prior amendments did not necessitate the new art rejection of claim 1. Original claims 2-4 were not subject to any art rejection in the Action dated 4/17/06. Claim 1 was amended to recite a Markush group consisting of the subject matter of claims 2-4. Hence, the present art rejection is a new rejection of the subject matter of original claims 2-4.

35USC112, first paragraph (written description)

The Action objects to the words "test" and "control". As recently restated by the Federal Circuit:

> In order to comply with the written description requirement, the specification "need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed." [cites omitted]
> All Dental Prodx, LLC v. Advantage Dental Prods, Inc., 309 F.3d 774, 779 (Fed. Cir. Oct 2002).

The invention is a method of determining cardiovascular risk in a person not predetermined to be subject to cardiovascular disease by determining the MIF concentration in the blood, saliva or urine of the person as a marker of cardiovascular risk for the person. The concept of a "marker of cardiovacular risk" implies to one skilled in the art that the marker is different in the risk group and in a corresponding control group. Furthermore, what you call the measure from the examined person ("test", "subject", etc.) and what you call the compared-to measure ("control", "predetermined value", etc.) are arbitrary and self-evident, inherent measures required for a disease "marker":

> The invention provides methods for characterizing an apparently healthy individual's risk of, and/or developing their risk profile for developing a future subject cardiovascular disorder. The method comprises obtaining a level of MIF in the individual, typically expressed as MIF concentration, and comparing the level of the marker to a predetermined value. The individual's risk or risk profile of developing a future subject cardiovascular disorder then is characterized based upon the level of the marker in comparison to the predetermined value. Specification, p.3, lines 14-20.

The recited predetermined value is a control:

> The predetermined value will depend upon the characteristics of the patient, and/or the relevant patient population. The predetermined value can be a single value, multiple values, a single range or multiple ranges. Thus, in one embodiment, the predetermined value is a plurality of predetermined marker level ranges, and the comparing step comprises determining in which of the predetermined marker level ranges the individual's level falls. In another embodiment, the predetermined value is a historical value from the patient. Specification, p.4, lines 11-16.

Though not required, the Specification even expressly refers to the compared-to or "predetermined value" a "control":

> I. Comparison of MIF and CRP levels as correlates to reductions in cardiovascular risk. This study was designed to compare MIF and CRP as markers correlating with cardiovascular risk.
>
> Methods: In an initial demonstration, we monitored MIF in obese adults, with very high cardiovascular risk, who were subjected to a one-year regimen of diet and exercise.
>
> Results: We found that MIF levels tracked progress (reduction in cardiovascular risk) through the treatment regimen better than did CRP. In our ***control*** group (n=83), MIF levels were 38 +/- 16 ng/ml. The obese patients at baseline are elevated to 100+ ng/ml generally and drop to normal levels generally after 1 year. Specification, p.5, line 7 (emphasis added)

That the determined MIF concentration is a "test", and the compared-to value is a "control" is both self-evident and inherent in the original claims. The issue for Written Description is whether the Specification reasonably conveys possession of the invention as claimed to those skilled in the art, and there is no evidence or argument of record that it fails to convey that possession.

35USC102(b)

Yabanuka et al. (Diabetes Care 2000, 23; 2, 256-58) "examined the concentration of serum MIF in type 2 diabetes to clarify the possibility that MIF is associated with the disregulation of glucose metabolism." p.256, sentence bridging cols. 1, 2 .

The authors report mixed findings: "The serum MIF level was elevated as the clinical stage of diabetic retinopathy advanced, but that was low in the proliferatiive stage (Fig.2). The serum MIF did not differ with the clinical stage of diabetic nephropathy and neuropathy." p.256, col.3, lines 16-22.

The authors speculate on possible explanations: "It is speculated that MIF stimulates insulin secretion and MIF secretion is regulated by glucose. It may be reasonable that MIF seems to modulate the carbohydrate metabolism as MIF modulates the inflammatory and immunological responses, counterregulating impaired homeostasis by the action of glucocorticoid suppression." p.257, col.2, lines 81-6.

The authors conclude that MIF is not a specific disease marker, but a nonspecific marker for illness in general: "Increased serum MIF may be another nonspecific marker for illness in general, rather than a key player in the pathogenesis of type-2 diabetes. In fact, MIF was increased in the sera of patients with uveitis and atopic dermatitis.... p.257, col.3, lines 12-17.

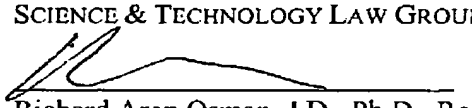
Claim 1 recites a method of determining cardiovascular risk in a person not predetermined to be subject to cardiovascular disease. The claim requires at least two steps: a first step of determining a test MIF concentration in the blood, saliva or urine of the person as a marker of cardiovascular risk for the person, wherein an elevated test MIF concentration compared with a control MIF concentration not associated with cardiovascular risk indicates that the person is subject to elevated cardiovascular risk; and a second step selected from the group consisting of: (a) assigning to the person a cardiovascular risk metric in accordance with the test MIF concentration; (b) prescribing for the person a cardiovascular treatment

modality in accordance with the test MIF concentration; and (c) making an additional assessment of cardiovascular risk of the person in accordance with the test MIF concentration, the additional assessment selected from the group consisting of a stress test, a CRP assay and an LDL assay.

Yabanuka et al. neither teach nor suggest the claimed two-step method. Yabanuka et al. do not suggest that MIF is a marker for cardiovascular risk. To the contrary, they suggest it is not useful as any specific disease marker, but rather is a non-specific marker for illness in general. The Action suggests anticipation of claim 1 wherein the second step is (a) "assigning to the person a cardiovascular risk metric in accordance with the test MIF concentration" (Action, p.4, last line); however, Yabanuka et al. nowhere teach or suggest assaying MIF as a marker for cardiovascular disease, and nowhere teach or suggest assaying MIF as a marker for cardiovascular disease, and then assigning to the subject person a cardiovascular risk metric in accordance with the assayed MIF concentration. Since Yabanuka does not teach or suggest assigning a cardiovascular risk metric in accordance with an assayed MIF concentration, the reference can not anticipate our claim.

Please charge our Deposit Account No.19-0750 for any necessary fee or extension of time (order UTSW:1477).

Respectfully submitted,
SCIENCE & TECHNOLOGY LAW GROUP



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